FIND

Because diagnosis matters

ACCELERATING DIAGNOSTICS USE TO PREVENT ANTIMICROBIAL RESISTANCE

AMR STRATEGY 2018

ABOUT FIND

FIND was founded in 2003 to bridge existing development gaps for essential diagnostics by initiating and coordinating research and development (R&D) projects in collaboration with the international research community, the public sector and the in vitro diagnostics industry. Today, FIND is a leading partner across the value chain of diagnostics development and delivery. We have programmes in tuberculosis and acute febrile respiratory infections, malaria and acute febrile syndrome, hepatitis C and neglected tropical diseases. We also have mini-portfolios in areas affecting reproductive and child health: HIV; sexually transmitted infections; and infections and nutritional deficiencies in children less than five years of age. At FIND, we envision a world where diagnostics guide the way to health for all people. We aim to turn complex diagnostic challenges into simple solutions to transform lives and overcome diseases of poverty. To do this we focus on four strategic goals throughout all the disease areas in which we work:

Catalyse development

Identify needed diagnostic solutions and remove barriers to their development

Guide use & policy

Lead products through the clinical trials pathway to global policy on use and market entry

Accelerate access

Support uptake and appropriate use of diagnostics to achieve health impact

Shape the agenda

Improve understanding of the value of diagnostics and strengthen commitment to their funding and use

FIND's Vision

A world where diagnosis guides the way to health for all people

FIND's Mission

Turning complex diagnostic challenges into simple solutions to overcome diseases of poverty and transform lives

“This is a global problem requiring multiple solutions – and accessible, accurate, and affordable diagnostics play a vital role in protecting our antibiotics and for surveillance in humans, animals, and the environment. I am pleased that organisations such as FIND are not only focusing on developing new diagnostics but also implementing existing ones in all parts of the world. Global leaders have recognised the importance of addressing antimicrobial resistance – but now it is time to act.”

Professor Dame Sally Davies, UK Chief Medical Officer, IACG on AMR co-convener

“...this is an issue of crucial importance for the entire human race – for people in developed and less developed countries alike. We must ensure that existing antibiotics remain effective, and that they are used only when medically necessary ...”

Statement by Federal Chancellor Angela Merkel at the 68th session of the WHO World Health Assembly in Geneva, 18 May 2015

“Antimicrobial resistance is a global health emergency that will seriously jeopardize progress in modern medicine. There is an urgent need for more investment in research and development, otherwise we will be forced back to a time when people feared common infections...”

Tedros Adhanom, Director-General, WHO, Call to Action on AMR, 17 October 2017

FOREWORD BY JIM O'NEILL

Antibiotics first entered common use in the 1950s, rightly perceived as wonder drugs as they truly transformed human and animal health. Today, their use has become ubiquitous and societies and economies are reaping the benefits. But bacteria, parasites and viruses are smarter than us. It is now clear that these pathogens will naturally evolve resistance to all our treatments. It is not an understatement to say that that could be catastrophic for humankind, as decades of medical progress are on the brink of being wiped out.

Action is not optional, and diagnosis is an essential weapon in our fight against antimicrobial resistance (AMR). It shocks me that the way in which we make prescribing decisions today hasn't fundamentally changed since the 1950s. There are many reasons for this, including a lack of good and rapid tests to confirm the judgement of the doctor, and the cost of such tests exceeding the price of the drugs, leading to "just in case" prescribing.

We need to stop treating antibiotics like candy. Yes, we need to ensure – especially in low- and middle-income countries – that everyone, humans and animals alike, get the appropriate drugs when they are really needed. But we need to stop behaving as though antibiotics are the miracle cure for virtually anything: from humans feeling a little under the weather, to fattening animals faster in order to increase farming productivity.

I had the pleasure of leading the 2016 *Review into Antimicrobial Resistance*[1], which identified interventions to address AMR that can boost supply of new treatments, for example by incentivizing research and development, and reduce demand for current treatments by decreasing unnecessary prescribing. Perhaps my single favourite of all the demand-reducing interventions focuses on two really powerful recommendations concerning diagnostics. First, we believe the Market Entry Awards that we proposed to stimulate the development of new antibiotics should be equally applicable to state-of-the-art diagnostic techniques. Second, we recommended that the richest countries, including all the G7 countries, should mandate into law that a validated diagnostic assay demonstrating the need for antibiotic therapy must be used prior to writing a prescription. Without such a big, bold step, it is unlikely that rapid progress can be made to reduce the scale of inappropriate use and limit the rapid emergence of resistance to our available drugs.

I thoroughly welcome the initiatives and strategies that FIND is proposing for the development and introduction of diagnostics to reduce the overuse of antibiotics and ensure that new drugs will remain effective for as long as possible. In the context of our Review's findings and recommendations, I believe these steps will move us in the right direction of reducing the scale of AMR globally.

1. Jim O'Neill (Review chairman). Tackling drug-resistant infections globally: final report and recommendations; the review on antimicrobial resistance. May 2016. https://amr-review.org

ABBREVIATIONS

AMR	Anti-microbial resistance
ARLG	Antibacterial Resistance Leadership Group
BARDA	United States Biomedical Advanced Research and Development Authority
CARB-X	Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator
CDC	United States Centers for Disease Control and Prevention
DNA	Deoxyribonucleic acid
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FIND	Foundation for Innovative New Diagnostics
GAMRIF	Global Antimicrobial Resistance Research Innovation Fund
GARD-P	Global Antibiotic Research and Development Partnership
GLASS	Global Antimicrobial Resistance Surveillance System
HIV	Human Immunodeficiency Virus
IACG	Inter-Agency Consultative Group
ICU	Intensive care unit
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
LMICs	Low- and middle-income countries
LRTI	Lower respiratory tract infection
MDR-TB	Multidrug-resistant tuberculosis
MRSA	Methicillin-resistant Staphylococcus aureus
NIH	National Institutes of Health
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
R&D	Research and development
ReAct	Action on Antibiotic Resistance
ReSeq	Relational Sequencing data platform
SDG	United Nations Sustainable Development Goal
STI	Sexually transmitted infection
TB	Tuberculosis
TPP	Target product profile
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
UTI	Urinary tract infection
WEF	World Economic Forum
WHA	World Health Assembly
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

EXECUTIVE SUMMARY

The inappropriate use of antibiotics and other medicines is fuelling the emergence of antimicrobial resistance (AMR) globally, and is reducing the effectiveness of the few treatment options we have left to treat severe bacterial illnesses. Currently, 700,000 deaths annually are due to drug-resistant strains of common bacterial infections, HIV and malaria and it is estimated that by 2050, 10 million deaths will be caused by AMR each year. Combatting AMR is crucial to achieve the United Nations Sustainable Development Goals (SDGs). Diagnostics are recognized as having a key role in both the Global Action Plan on Antimicrobial Resistance (WHO) and the AMR Framework for Action supported by the IACG. Diagnosis as the 'first prescription' has proved its ability to reinforce antimicrobials as a 'global good', to ensure patient health and to promote economic resources.

FIND's AMR strategy is focused on halting and preventing antimicrobial resistance to save lives by 1) optimizing use of antimicrobials; 2) preserving new drugs; and 3) empowering surveillance efforts.

FIND will work closely with its partners to address the main barriers to diagnostic solutions for AMR by contributing to the development of "fit-for-purpose" diagnostic tests, to evidence collection for policies and guidance on use, and to improved access to diagnostics in countries. FIND plans to build an existing resistance portfolio in tuberculosis, malaria and non-malarial fever, where significant progress has been made with rapid and near-patient molecular and immunoassays. Current open access resources, notably specimen banks and databases, will be expanded to accelerate AMR assay development and regulatory approval.

To achieve these objectives, the following interventions have been prioritized for the current strategic period:

1. **Optimize use of antimicrobials through triaging tools for community-acquired infections, such as febrile illnesses, respiratory or urinary tract infections: Catalyse the development, evaluate the utility fo r low- and middle-income countries (LMICs) and create models for uptake of simple and rapid diagnostic solutions, including decision aid software, to improve rational use of antimicrobials and optimal management of patients when they first present.**

2. **Preserve new drugs through companion diagnostics for new antibiotics: Support the development and use of complementary rapid diagnostics, starting with those for gonorrhea, to prevent overuse and early emergence of resistance.**

3. **Enable national and global surveillance through fully-interconnected diagnostic networks: Provide connectivity and data interpretation to attain the full value of diagnostic data for patients and systems management, and deliver real-time surveillance based on routine hospital and community data.**

The ultimate impact of FIND's work will depend on the uptake of such diagnostic solutions. As there is currently no established mechanism to drive access to innovation in LMICs, FIND will strongly advocate and seek partners for the creation of an AMR Diagnostics Use Accelerator that could create a pull mechanism for further R&D investment. LMICs carry the highest AMR burden, so global impact can only be achieved by targeting these populations and investing in diagnostic services that are scalable in these settings.

AMR CHALLENGES AND OPPORTUNITIES: GLOBAL AND LOCAL

The inappropriate use of antibiotics and other medicines is fuelling the emergence of antimicrobial resistance (AMR) globally, and is reducing the effectiveness of the few treatment options we have left to treat severe bacterial illnesses. Currently, 700,000 deaths annually are due to drug-resistant strains of common bacterial infections, HIV and malaria and it is estimated that by 2050, 10 million deaths will be caused by AMR each year – with a loss of over 100 trillion USD in economic output[2]. In 2015 alone there were almost 500,000 new cases of multi-drug resistant tuberculosis reported[3]. A major cause of neonatal deaths worldwide, sepsis is often caused by resistant bacteria.

Addressing the spread of AMR is essential to achieving the United Nations Sustainable Development Goals (SDGs). In addition to good health and well-being (SDG 3), AMR also threatens sustainable food production (SDG 2), clean water (SDG 6) and economic improvement (SDG 1 and 8).

AMR does not discriminate. The most vulnerable populations are most at risk for contracting life threatening infections. In particular, people living in LMICs are significantly affected by high rates of AMR, as indiscriminate use of antibiotics – a major driver in the development of drug resistance – to treat non-bacterial infections is common due to the fact that doctors and health care providers often rely on empirical evidence, even for 2nd and 3rd line antibiotics, due to a lack of accessible and usable diagnostic tests.

In the absence of appropriate diagnostics, we have seen a 40% increase in the global consumption of antibiotics in a single decade[2]. There is a clear observed correlation between antibiotic overuse and resistance. In LMICs, most children with fever and a negative malaria test are estimated to receive antibiotics (e.g. 60-95% in a study carried in Tanzania), while only a very small share of them would actually need them, as the majority of these cases are self-limited viral illnesses.

The issue of how to fight AMR has been on the global public health agenda for some time, yet it has only recently been raised to a crisis level, with increasing political momentum[4] and global attention[5]. At the same time there has been as a growing recognition of the benefits that diagnostics can bring to many of the identified core action areas[2].

2. O'Neill J. "Tackling Drug-Resistant Infections Globally: Final Report and Recommendations". May 2016 https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

3. WHO. Global Tuberculosis Report, 2017. https://amr-review.org/

4. G20 Health Ministers' Meeting: Fighting Antimicrobial Resistance, Berlin, 20 May 2017 http://www.oecd.org/g20/summits/hamburg/g20-health-ministers-meeting-fighting-antimicrobial-resistance.htm

5. AMR Framework for Action Supported by the IACG, August 2017 http://www.who.int/antimicrobial-resistance/interagency-coordination-group/20170818_AMR_FfA_v01.pdf

DIAGNOSTICS: A CRITICAL COMPONENT OF AMR SOLUTIONS

Diagnosis allows us to protect not just our critical drug arsenal, but also patients who are under threat from resistant pathogens. Diagnosis as the 'first prescription' has proven its ability to save antibiotics, health and money. A number of studies show that antibiotic use can be dramatically cut through the use of a simple diagnostic and there is increasing evidence that limiting overuse of antibiotics can have positive impact on individual patient outcomes[6,7,8,9,10,11,12]. Diagnostics have been shown to reduce the time to pathogen identification and to optimal and effective antimicrobial treatment; active surveillance testing can lead to significant cost savings[13,14,15].

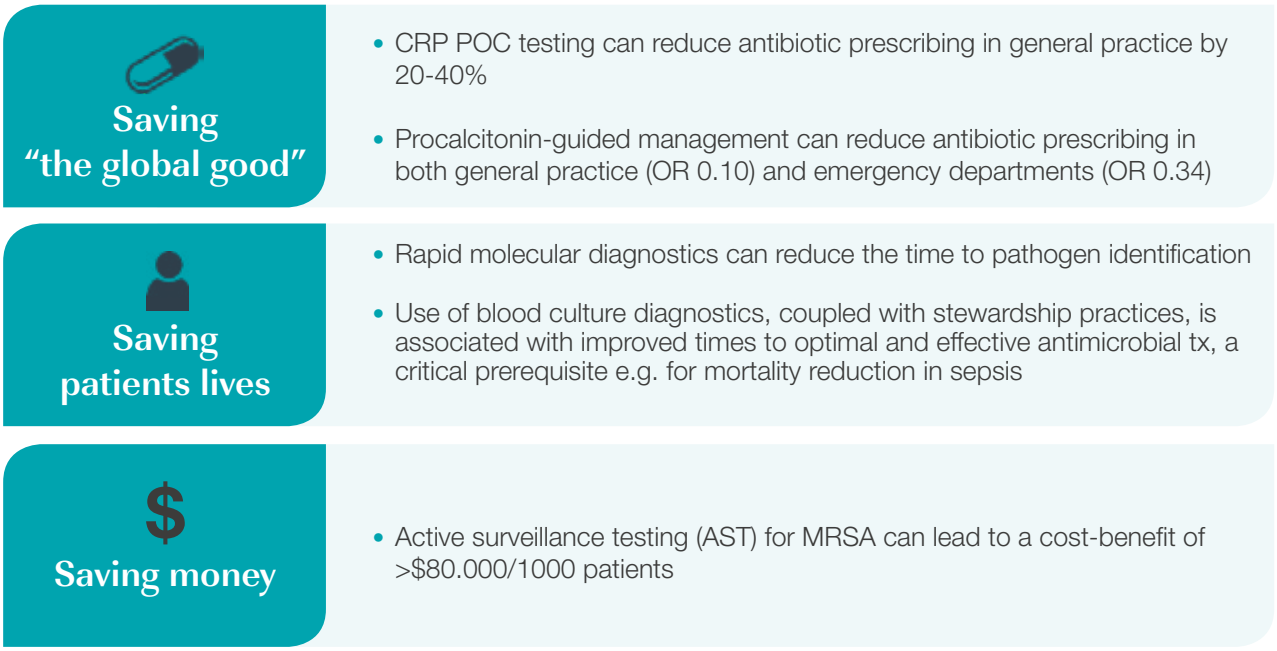

Figure 1: Diagnosis as the first prescription.

6. Nga et al., "Point-of-care C-reactive protein testing to reduce inappropriate use of antibiotics for non-severe acute respiratory infections in Vietnamese primary health care: a randomised controlled trial", *Lancet Glob Health*, August 2016

7. Lubell et al., "Modelling the Impact and Cost-Effectiveness of Biomarker Tests as Compared with Pathogen-Specific Diagnostics in the Management of Undifferentiated Fever in Remote Tropical Settings", *PLoS ONE*, March 30, 2016

8. Lowe et al., "Targeted Antimicrobial Stewardship Intervention for Inpatients with Viral respiratory tract infections." *Open Forum Infectious Diseases*. Vol. 3. No. suppl_1. Oxford University Press, 2016.

9. "White paper on Rapid Diagnostics Technologies to Tackle Antimicrobial Resistance", https://healthfirsteurope.eu/wp-content/uploads/2015/05/White-Paper-on-rapid-diagnostic-technologies-to-tackle-AMR.pdf,, Health First Europe, 2017

10. Tonkin-Crine et al., "Clinician-targeted interventions to influence antibiotic prescribing behaviour for acute respiratory infections in primary care: an overview of systematic reviews." *Cochrane Review*

11. Conway et al., "Recurrent Urinary Tract Infections in Children – Risk factors and association with prophylactic antimicrobials", *JAMA*, 2007

12. Brismar et al., "Comparative effects of clarithromycin and erythromycin on the normal intestinal microflora." *Scan. J Infect Dis* 23.5 (1991); Buffie et al., "Profound alterations of intestinal microbiota following a single dose of clindamycin." *Infect Immun* 80.1 (2012); Sekirov, Inna, et al., "Antibiotic-induced perturbations of the intestinal microbiota alter host susceptibility to enteric infection." *Infect Immun* 76.10 (2008); Teo et al., "The infant naso-pharyngeal microbiome impacts severity of lower respiratory infection and risk of asthma development." *Cell Host Microbe* 17.5 (2015); Boursi et al., "The effect of past antibiotic exposure on diabetes risk." *Eur J Endocrin* 172.6 (2015).

13. Banerjee et al., "Randomized trial of rapid multiplex polymerase chain reaction-based blood culture identification and susceptibility testing. *Clin Infect Dis* 2015;61:1071

14. Messacar et al., "Clinical Impact and Provider Acceptability of Real-Time Antimicrobial Stewardship Decision Support for Rapid Diagnostics in Children With Positive Blood Culture Results", *J Pediatric Infect Dis Soc*, 2016

15. Peterson et al., "Methicillin-Resistant Staphylococcus aureus Control in the 21st Century: Laboratory Involvement Affecting Disease Impact and Economic Benefit from Large Population Studies." *J Clin Microbiol*, 2016

Optimizing use of antimicrobials

The overuse of antibiotics is often linked to their use in treating non-bacterial infections, predominantly when patients present with generalized symptoms such as acute fever, lower respiratory tract infections, urinary tract infections, sexually transmitted infections or diarrhoea. A U.S. study showed that two-thirds of the 40 million people who are given antibiotics for respiratory issues annually receive them unnecessarily[16].

Diagnosis enables the rapid selection of the most appropriate therapy. It can also reduce the length of time a patient may be treated empirically, either with ineffective or unnecessary antimicrobials. Rapid susceptibility diagnosis allows for prompt escalation or de-escalation of antibiotic therapy, and switches between first-, second- and third-line treatment options. For example, the use of blood culture diagnosis is associated with improved time to optimal and effective antimicrobial therapy and a decrease in unnecessary antimicrobial use in children . In addition, given the substantial problems around antibiotic quality, national quality assurance programmes that are equipped with the right technologies can detect counterfeit or sub-standard antibiotics.

The public health benefit of reducing the inappropriate use of antibiotics is directly linked to reducing the selective pressure that drives the emergence of resistance.

Preserving new drugs

Stewardship of current and new antibiotics is paramount to ensuring they retain their efficacy for as long as possible, especially for critically needed treatments, e.g., for gram-negative bacteria like N. gonorrhoea. Resistance will naturally emerge to any new drug but the early introduction of a gating diagnostic will ensure that these drugs are used appropriately, shielding them from rapid overuse and early emergence of resistance. This protection of new drugs should slow the emergence of resistance and preserve this global resource.

Empowering surveillance efforts

Connected surveillance tools to track and map emergence, geographical patterns and range across pathogens of resistance are the basis of national and global surveillance programmes such as the Global Antimicrobial Resistance Surveillance System. They enable appropriate control measures at local, national and global levels, as well as improved treatment strategies. Screening and isolation of infected patients help prevent the spread of resistant pathogens in community and hospital settings. Sharing of information on the emergence of resistance at the national, regional and global level helps to set guidelines and drive prioritization of both development and access activities.

Beyond these three critical areas, the role of diagnostics to combat AMR is evident across every category set out in the IACG Framework for Action (Table 1).

16. Data extracted from: Shapiro et al., "Antibiotic prescribing for adults in ambulatory care in the USA, 2007.09." J*ournal of Antimicrobial Chemotherapy*, 2013

17. Messacar et al., "Clinical Impact and Provider Acceptability of Real-Time Antimicrobial Stewardship Decision Support for Rapid Diagnostics in Children With Positive Blood Culture Results", *J Pediatric Infect Dis Soc*, 2016

Table 1: Diagnostics underpin each of the IACG Framework for Action content areas.

Reduce need and unintentional exposure	Human infection prevention and control	✓	Identification of resistant pathogens
	Clean water and sanitation	✓	Identification of source contamination
	Clean water and sanitation	✓	Identification of resistance; surveillance of zoonotic transmission events
	Food safety	✓	Identification of contaminants
	Environmental contamination	✓	Quantify antibiotics
Optimize use of medicine	Human use	✓	Rapid triaging, infection and resistance identification
	Animal & agricultural use	✓	Identification of pathogens
	Laboratory capacity & surveillance	✓	Identification of pathogens and resistance
Invest in innovation, supply and access	Basic research	✓	Biomarker discovery
	Development of therapeutics & access	✓	Efficacy measurement, Stewartship of new therapeutics
	Diagnostics development and access	✓	Applies to all
	Vaccine development and access	✓	Efficacy measurement, Rapid identification for deployment
	Quality	✓	Counterfeit drug detection

FIND'S STRATEGY IN AMR

Acknowledging the pivotal role of diagnostics in safeguarding antibiotics as a global good, patient lives and country resources, FIND has developed a strategy that focuses on halting and preventing AMR by targeting three discreet challenges:

- **optimizing use of antimicrobials;**
- **preserving new drugs; and**
- **empowering surveillance efforts.**

To achieve this, FIND will draw on its existing operating model as well as on new initiatives in an end-to-end effort in which product development is complemented with work on policy initiatives and access (Figure 2). The planned results of our work within the next years are that antibiotic use will be underpinned by results of simple tests that are deployed in stewardship strategies especially for new drugs, and are fully interconnected for robust surveillance. While working on global R&D solutions, we will target LMICs for access work. Given the dynamic nature of AMR and its rapid spread across borders, addressing the problem in LMICs is expected to have global impact, as these countries carry the highest AMR burden and have the most challenging access issues.

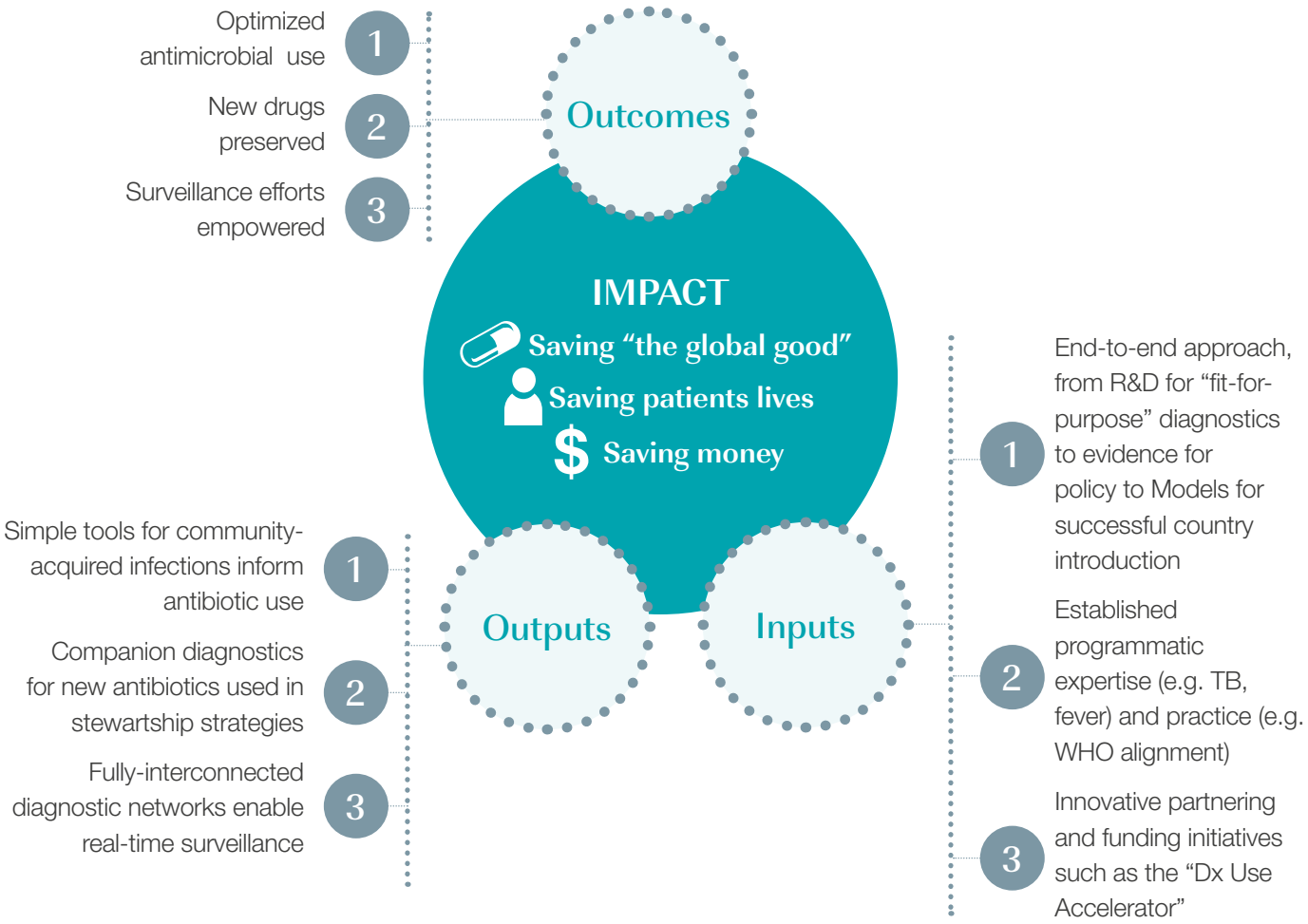

Figure 2: FIND's strategy to achieve impact in AMR.

FIND interviewed ~30 experts and stakeholders to help identify priority AMR needs and barriers outside of the vertical programmes for TB, malaria and HIV. Aside from identifying an important need for R&D, it was noted that, more importantly, barriers to uptake must be lifted. In LMICs, some diagnostics may not be in use because they are either unavailable or too expensive for these markets. Others have no data supporting their use in LMICs, which further hinders their uptake and appropriate market pricing. The low demand and resulting low industry investment is complicated by the lack of a global health purchasing entity, like the Global Fund, especially given the cross-cutting nature of AMR.

While typical LMIC market dynamics hamper access to available diagnostics, there is a larger problem in terms of AMR diagnostics. In nearly all cases, it is cheaper and simpler to treat a patient with antibiotics than to test a patient with a diagnostic. Antibiotics are generally unregulated and easily available. Since patients are mostly responsible for their own health care costs, it will be a challenge to convince them to pay for a testing and treatment, especially when the diagnostic part will likely be several factors more expensive than the drugs. Compounding this complication is the facility of providing an antibiotic. The doctor or health care provider may feel they have provided good care by giving antibiotics and the patient in turn feels well cared for. This is particularly important in rural settings where patients cannot always get hold of medical advice and where follow-up visits may not be feasible even in the case of increasing severity.

FIND's strategic activities aim to respond to the main identified barriers that affect the impact of diagnostic solutions (Figure 3).

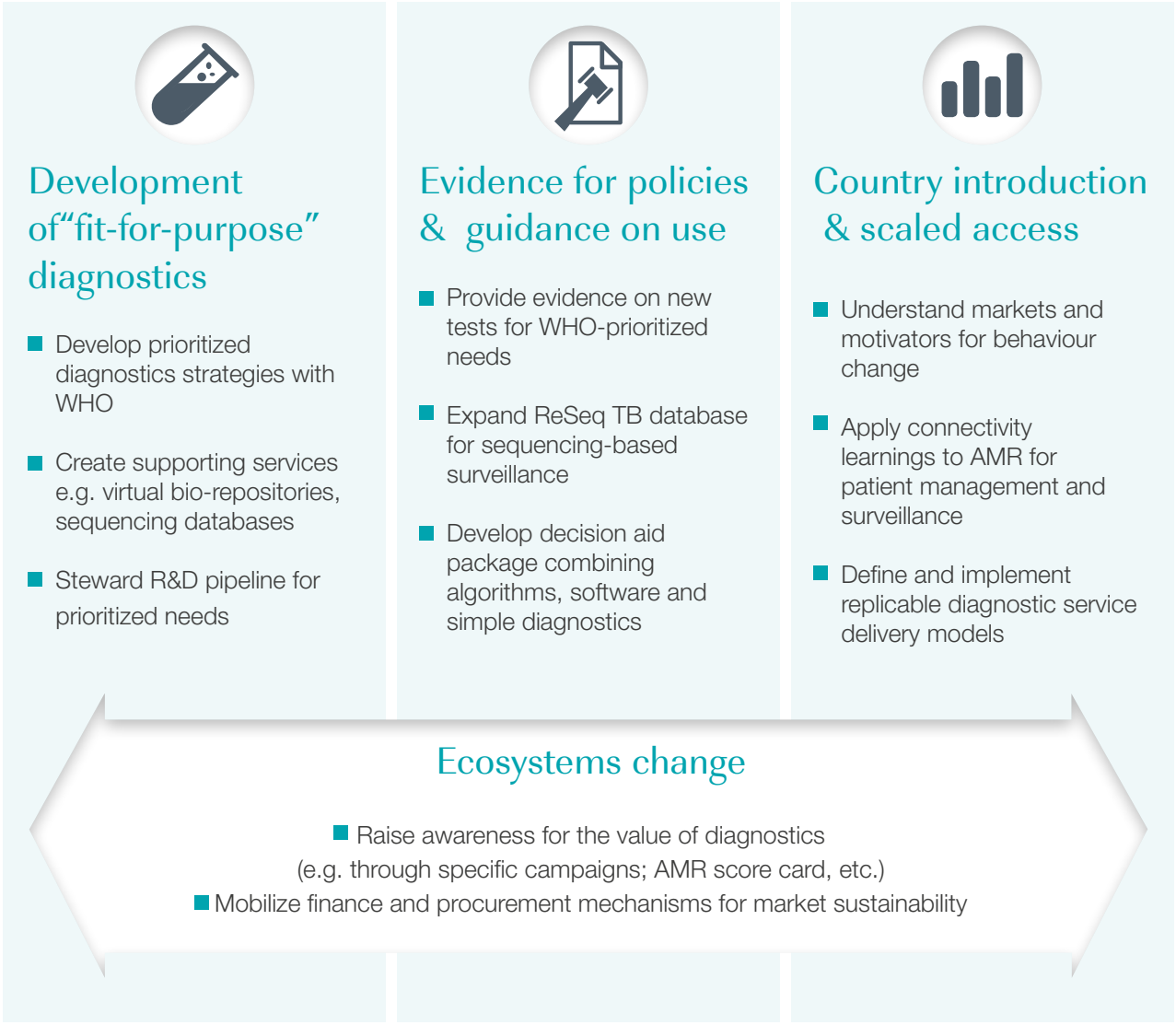

Figure 3: Solutions across the value chain to address barriers limiting access to and use of diagnostics.

PRIORITY INTERVENTIONS FOR IMPACT

To date, FIND's work in AMR has focused on tuberculosis, malaria and Fever; notably the development, evaluation and introduction of rapid molecular and sequencing-based solutions for drug susceptibility testing and point–of-care triaging tools.

By analysing the patient pathway and the diagnostic information that is needed at different levels of the health system, we narrowed down eight priority interventions and ranked them in terms of short-term action (Figure 4).

	Identified scenarios	Key needs	Diagnostic readiness	Impact: Antibiotic use	Impact: Lives saved	Role for FIND	R&D	Policy & Access
★	1. Fever and/or LRTIs	**R&D:** develop triaging tools **Pol. & Acc.:** Evaluate dx packages: e.g., CRP; Procalcetonin; CBC; mol panels	+++	++++	+++	+++	1	1
★	2. UTIs	**Pol. & Acc.:** Evaluate urinary dipsticks and define route-to-market	++++	++++	+	+++	3	1
	3. Diarrhoea	**Pol. & Acc.:** evaluate rota/ adenovirus RDTs, multiplex molecular test	+++	+++	++	+++	3	3
	4. New-borns with suspected severe infection	**R&D:** tbd **Pol. & Acc.:** evaluate procalcetonin; Blood culture; CBC; oximeters	+	++++	++++	+	2	2
★	5. STIs	**R&D:** improve gonorrhoea DST, new RDTs and multiplex molecular tests Pol. & Acc.: define route-to-market	++	++	++	++	1	2
★	6. Quality Diagnostics to identify counterfeits	**R&D:** tbd **Pol. & Acc.:** evaluate Minilab, CD3, Raman/NIR	+	+++	+++	+++	2	2
★	7. Patients with resistant pathogens	**Pol. & Acc.:** evaluate molecular screening of swabs or isolates	++	+++	++	++	3	1
★	8. Surveillance data, tools and processes	**R&D:** develop connectivity solutions Pol. & Acc.: integrate existing solutions into national surveillance	N/A	++++	++	+++	3	1

Figure 4: Preliminary prioritization of needs (1 = highest priority, stars indicating areas of near term focus) based on existing and relevant tools to address identified scenarios.

Taking the outcomes of the analysis and applying the findings towards our strategic objectives, FIND will expand its existing portfolio to address the following priority needs:

Optimizing use of antimicrobials

Triaging tools for community acquired infections such as febrile illnesses, respiratory or urinary tract infections
Catalyse development, evaluate utility for LMICs and create models for uptake of simple diagnostic solutions, including decision aid software, to improve rational use of antimicrobials and optimal management of patients when they first present

Preserving new drugs

Companion diagnostics for new antibiotics:
Support the development and use of complementing diagnostics for new antibiotics, starting with those for gonorrhea, to prevent overuse and early emergence of resistance.

Empowering surveillance efforts

Fully interconnected diagnostic networks:
Provide connectivity and data interpretation solutions to achieve the full value of diagnostic data for patients and systems management, and to supply real-time surveillance based on routine hospital and community data.

Figure 5: Three priority diagnostic interventions to contribute to WHO Global Action Plan

Triaging tools for community acquired infections

One of the most promising solutions for triaging patients in the community that present with fever or other common symptoms like cough or diarrhoea would be a test based on host biomarker detection to differentiate between bacterial and non-bacterial infections. Through an extensive, publicly available landscape analysis, FIND has identified a number of biomarkers for fever that could be used in rapid blood testing in low- and middle-income countries. In 2017, FIND started a multi-centric study to evaluate the performances of potential new biomarkers to differentiate bacterial from non-bacterial febrile illnesses of outpatients from hospitals in three countries.

To prevent the use of unnecessary antibiotics, FIND plans to expand this triaging programme to evaluate the utility of simple triaging tools (e.g. UTI dipsticks, electronic health algorithms), redesign or adapt them for LMIC needs and develop models for uptake to optimize the use of antimicrobials.

Companion diagnostics for new antibiotics

FIND aims to support the continued efficacy of new antimicrobials. An initial priority could be the development of diagnostics to improve better rapid gonorrhoea tests and resistance testing to enable a definitive diagnosis prior to treating patients with new antibiotics that are currently in development. These tests will ensure that only patients with gonorrhoea or drug-resistant gonorrhoea receive the new treatment, thereby preventing overuse and early emergence of resistance. It is estimated that introducing a point-of-care rapid test for gonorrhoea could significantly reduce the use of ceftriaxone and shorten the mean time to treatment by 2.3 days[18].

Data utilization for clinical decision-making and surveillance

Ensuring connectivity, i.e., linking diagnostic tests with communications technology, allows for better management of health data and maximizes the health impact of the tests. Connectivity solutions help strengthen the link between patient diagnosis and treatment. The real-time transmission of geo-tagged test results to national health information systems means that potential AMR cases can be addressed immediately, allowing for a rapid response. FIND plans to establish connectivity for AMR diagnostics and decision aid tools, thereby extending the reach of national surveillance programmes to include routine hospital and community data. In addition, remote monitoring can improve supply chain management and forecasting and enhance diagnostic device quality assurance.

18. A study conducted in Tanzania among acute febrile children shows that 70.5% of the children had a viral disease, 22.0% had a bacterial disease and 10.9% had a parasitic disease.

OPERATING MODEL

FIND works as a bridge between experts in technology development, policy, and clinical care and has active collaborations with over 200 partners. FIND will work closely with WHO to support the development of TPPs, provide input on policy recommendations and guidelines and inform global surveillance efforts. Diagnostics are usually a minor component of existing initiatives such as CARB-X, JPIAMR, NIH, BARDA, Bill & Melinda Gates Foundation, and ARLG and there is currently no mechanism that supports interventions to drive uptake of existing and new diagnostics to combat AMR. FIND will i) collaborate with existing and new partners to support an integrated response to AMR (Figure 6); ii) advocate for the creation of an AMR Diagnostics Use Accelerator to establish a smooth pathway to uptake of diagnostics in LMICs; and iii) create a pull mechanism for R&D investment by creating market predictability. Through an Accelerator, cross-cutting issues such as market and pricing interventions; procurement mechanisms; policy change; information, education and communication for behaviour change and civil society engagement; and knowledge management could be most appropriately and usefully addressed.

Figure 6: FIND's role in possible collaborations with key partners in the AMR response.

Results and impact of the different interventions will be monitored through robust and standardized processes, and results widely disseminated through partnering networks and other channels.

A step-change in diagnostic use is possible, as has been demonstrated for malaria and HIV where we have seen a rapid transformation of the diagnostics landscape in LMICs within a decade. Change for AMR will rely on strong partnerships and coordination. Funding for scalable and innovative interventions to overcome barriers and accelerate diagnostic impacts is critical.

In combination, our priority interventions will save global goods by prolonging the life span of existing diagnostics, save health by ensuring better and timelier treatment, and save money both by reducing the use of antibiotics and the health impact of antibiotic resistance.

INVESTMENT NEED

FIND recognizes the burden caused by drug resistant TB, HIV and malaria, and their role in contributing to the global AMR challenge. However, the focus of this investment case will specifically be on pathogens and syndromes not already addressed in existing programmes.

FIND's AMR strategy will require a funding commitment of ~$72M to drive the work divided into three phases spanning the first six years, while expecting a 10-year programme lifecycle (additional funding to be identified in the later phases). Phases have been structured so that key deliverables must be completed to allow for next phase prioritization and maturation of the initiative. Support for the WHO's Essential Diagnostics List will be a priority during Phase 1 and Phase 2 to ensure alignment and clarity on priorities.

Phase 1: Launch of AMR Strategy | **Years: 2018 - 2019** | **Funding Commitment: $17M**

Phase 1 will focus on establishing the key partnerships and aligning on priorities in AMR beyond fever. Market understanding on the impact of diagnostics in AMR will be established and priority activities will be implemented across development, policy, and access. An R&D portfolio will be built for at least two priority target product profiles. Prioritized clinical scenarios, publication of landscapes and TPPs, and establishing a virtual sample bank and a decision-aid package combining algorithms, software and simple diagnostics will demonstrate early impact. Multi-centre studies will be conducted to demonstrate impact of at least three triaging tools. Study data and support for the WHO Essential Diagnostics List will inform priorities for Phase 2 as the work begins to expand.

Phase 2: Implement & Expand | **Years: 2020 - 2021** | **Funding Commitment: $30M**

n Phase 2, the strategy will mature into established pipelines encompassing existing and emerging tools with investments into an expanded R&D portfolio, including two new priorities. Demonstration studies for at least four emerging diagnostic tools will demonstrate impact. Focus on expanding the ReSeq database to standardize resistance profiles for pathogens beyond TB will support global development and surveillance efforts in the fight against AMR. At least two replicable service delivery models will be defined and implemented across three to five countries to ensure uptake of solutions. In-country champion networks will be established to facilitate change at the local and national levels and ensure a sustainable hand-off of projects once they are completed. Connectivity solutions will be linked to AMR to facilitate local-to-global communication, data sharing and response to AMR.

Phase 3: Continue at scale | **Years: 2022 - 2023** | **Funding Commitment: $25M**

Phase 3 will continue to mature R&D portfolios and deliver three new diagnostic solutions while intensifying activities and in-country demonstrations to drive policy change, and to ensure uptake and adoption of game-changing diagnostics. The work started in Phase 1, and continued in Phase 2, around the establishment of a virtual sample bank will be matured to enable the development of emerging technologies. Definition and demonstration of additional replicable service delivery models in at least three countries will ensure impact of the developed solutions. New initiatives and opportunities will be clearly defined to inform how the strategy should evolve into Phase 4 to support the global needs in AMR.

NEXT STEPS

FIND's fever programme, which includes some of the targeted activities here, is well underway, and broader TPP and landscaping work has started. Establishing and operationalizing partnerships will be among the initial priorities. Please reach out to **catharina.boehme@finddx.org** and **cassandra.kelly@finddx.org** if you are interested in partnering with us on this important programme.

Photo credits:
Cover: Ben Phillips
Page 17: Ben Phillips

Production and editing: FIND Communications
Design and layout: Minthical

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ACCELERATING DIAGNOSTICS USE
TO PREVENT AMR